REMARKS

Claims 20-41 are pending. Independent Claim 20 tracks and finds support in original claim 5. Claims 27 and 28 find support in the specification on page 6, line 6 and original Claim 5. The cytokines of Claims 29-34 are described in original Claim 9. The culture supernatants of Claims 35-36 find support in original Claims 10 and 11 and Claim 37 in original Claim 12. Claims 38-40, directed to screening methods, and Claim 41, find support in original Claims 13-17 and in the specification at page 7, lines 18-*et seq*. Accordingly, the Applicants do not believe that any new matter has been added. Favorable consideration is requested.

Restriction/Election

The Applicants note that the restriction requirement has now been made FINAL. The Applicants respectfully request that the claims falling into the nonelected groups, which depend from or include all the limitations of those of elected Group I, be rejoined upon an indication of allowability for the elected claims, see MPEP 821.04.

Objection to the Specification

The specification was objected to as containing sequence disclosures but as failing to comply with the requirements of 37 C.F.R. § 1.821 through 1.825. Applicants submit that these objections are moot in view of the substitute sequence listing appended herewith.

Applicants are submitting a Sequence Listing and a corresponding computer-readable Sequence Listing with the application filed herewith. The sequence information recorded in the corresponding computer-readable Sequence Listing is identical to the paper copy of the Sequence Listing.

Rejection—35 U.S.C. 112, second paragraph

Claims 1-6 and 8-11 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite. The Applicants submit that these rejections are moot in view of the cancellation of these claims. They would not apply to the present claims for the following reasons:

The term "osteoclast precursor cell" is well known in the art and is described in the specification, for instance, on page 5, lines 1-16. Moreover, the isolation of such cells is exemplified on page 8, starting at line 22. The specification also exemplifies differentiating osteoclast precursor cells into osteoclasts and then isolating osteoclasts as shown in Examples 1 and 2 as well as Fig. 1 and 2. As exemplified, a differentiated osteoclast precursor cell is an osteoclast. The term "eotaxin-3" which also now appears in claim 1, is well known in the art as shown by the attached abstract (Gene Bank: Accession No. E28836). Accordingly, the Applicants respectfully request that these rejections now be withdrawn.

Rejection—35 U.S.C. 102(e)

Claim 1 was rejected under 35 U.S.C. 102(e) as being anticipated by Moore, U.S. Patent No. 5,830,682. This rejection is moot in view of the cancellation of Claim 1. This rejection would not apply to new Claim 20, which is directed to culturing hematopoietic stem cell derived cells, optionally in the presence of serum, but in the absence of any additional cytokines.

Rejection—35 U.S.C. 102(b)

Claims 1, 5, 6 and 8 were rejected under 35 U.S.C. 102(b) as being anticipated by Purton et al. [U], Biosis Accession No.1996:49634 (abstract). The method of Purton requires the treatment (or mobilization) of peripheral blood mononuclear cells (PBMC) with

granulocyte colony-stimulating factor (G-CSF) to increase the frequency of osteoclast precursor cells, see the title of this abstract. Namely, this method is conducted in the presence of G-CSF, an added cytokine.

In contrast, the methods of Claims 20 and 26 involve osteoclast precursor cells obtained by culturing cells in the absence of added cytokines, such as G-CSF. Moreover, Purton teaches away from the present invention by disclosing that comparable osteoclast formation was not detected in cultures of normal marrow or normal nonmobilized peripheral blood. Accordingly, the Applicants respectfully request that this rejection now be withdrawn.

Rejection—35 U.S.C. 102(b)

Claims 2, 5, 6, 8 and 9 were rejected under 85 U.S.C. 102(b) as being anticipated by Matayoshi et al. [V], PNAS (USA) 93:10785. This rejection is moot in view of the cancellation of these claims. It would not apply to new Claims 20-41 for the following reasons. Matayoshi treats or mobilizes hematopoietic stem cell precursors with a cytokine. Matayoshi et al. disclose a method for preparing osteoclast cells directly from purified, G-CSF mobilized, $CD34^+$ hematopoietic precursor cells which are not osteoclast precursor cells. Namely, in this method, the presence of osteoclast precursor cells is not confirmed. Moreover, the culturing $CD34^+$, Stro-1 cells is conducted in the presence of GM-CSF, IL-1 and IL-3. Thus, unlike the methods of the present claims, the method of Matayoshi is conducted in the presence of added cytokines. Accordingly, the Applicants respectfully request that this rejection be withdrawn.

Rejection—35 U.S.C. 103

Claims 1- 6 and 8-11 were rejected under 35 U.S.C. 103(a) as being unpatentable over Matayoshi et al. [V], PNAS (USA) 93:10785 taken with Purton et al. [U], Biosis Accession No.1996:49634 (abstract); Moore, U.S. Patent No. 5,830,682 [A]; Torok-Storb et al., U.S. Patent No. 5,879,940 [B]; and Lorenzo et al. [W], Endocrinology 121:1164. This rejection is moot in view of the cancellation of these claims. It would not apply to new Claims 20-41 for the following reasons.

Matayoshi and Purton have both been addressed above and do not suggest producing osteoclast precursor cells by culturing cells from peripheral blood or joint fluid without added cytokines, such as G-CSF.

Moore, Torok-Storb, and Lorenzo do not suggest producing osteoclast precursor cells by culturing cells from peripheral blood or joint fluid without added cytokines, such as G-CSF.

Moore is directed to a method for immortalizing cells by infection with retrovirus and does not disclose or suggest isolation of osteoclast precursor cells by culturing cells from peripheral blood or joint fluid without added cytokines, nor a method for differentiating osteoclast precursor cells into osteoclasts.

Torok-Storb teaches that a supernatant of phytohemagglutinin-stimulated human blood peripheral mononuclear cells contains osteoclast activating factor which stimulates differentiation of osteoclast precursor cells. Moore discloses a method for preparation of cells immortalized by infection with retrovirus, but does not teach a method for isolating osteoclast precursor cells or a method for differentiating osteoclast precursor cells in the absence of cytokines.

Accordingly, the Applicants submit that this rejection would not apply to the present claims.

Rejection—35 U.S.C. 103

Claims 1- 6 and 8-11 are rejected under 35 U.S.C. 103(a) as being unpatentable in view of Kitaura et al. [X], Foreman et al. [U-1], Onoe et al. [W-1] and Dahl et al. (V-l). This rejection is moot in view of the cancellation of these claims and would not apply to new Claims 20-41 for the following reasons.

Kitaura et al. [X] disclose that the cDNA and deduced as sequences, chromosome location, RNA distribution, functional expression and receptor selectivity for human eotaxin, but not the activity of eotaxin for differentiating osteoclast precursor cells.

Foraman et al. [U-1] disclose that the deduced as sequences, functional, expression, chemoattractant and receptor selectivity for human eotaxin-2, but not the activity of eotaxin for differentiating osteoclast precursor cells.

Onoe et al. [W-1] disclose that IL-7 did not induce bone resorption, but not the activity of IL-7 for differentiating osteoclast precursor cells.

Dahl et al. [V-1] disclose hyaluronic acid production *in vitro* by synovial lining cells from normal and rheumatoid joints, but neither the method for isolating osteoclast precursor cells, nor the method for differentiating osteoclast precursor cells is disclosed. Accordingly, the Applicants respectfully submit that this rejection does not apply to the present claims.

CONCLUSION

In view of the above amendments and remarks, the Applicants respectfully submit that this application is now in condition for allowance. Early notification to that effect is earnestly solicited.

Respectfully submitted,

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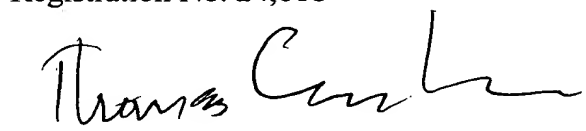

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MARKED UP COPY OF AMENDMENT

IN THE CLAIMS

Cancel Claims 1-19.

Add new Claims 20-41:

--20-41. (New)--